UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Offic
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

#C

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/177,814	10/23/98	GILTON T	3530US(97-12

HM22/0721

JOSEPH A WALKOWSKI
TRASK BRITT & ROSSA
P O BOX 2550
SALT LAKE CITY UT 84110

EXAMINER	
GABEL,G	
ART UNIT	**PAPER NUMBER**
1641	3

DATE MAILED: 07/21/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/177,814	Gilton
Examiner	**Group Art Unit**
Gailene R. Gabel	1641

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-110* is/are pending in the application.

Of the above, claim(s) *75-104 and 108-110* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-74 and 105-107* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims *1-110* are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 2

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-74 and 105-107, drawn to an chromatographic separation apparatus with flow channel device, classified in class 210, subclass 659.

II. Claims 75-88 and 108-110, drawn to method of fabricating a separation device with ultrasmall channel device, classified in class 210, subclass 656.

III. Claims 89-104, drawn to method of isolating a constituent of a sample, classified in class 436, subclass 161.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the process of micromachining in Group II can be used to fabricate thermally-activated chemical filters with reaction chambers and electrodes, incorporated therein, to control the flow of electrically charged chemicals.

Inventions I and III are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another

materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case, the process in Group III can be performed using two-phase aqueous partitioning systems wherein a liquid sample is introduced into solutions with phase forming elements, thereby causing a desired analyte to be separated or isolated.

Inventions II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operations and functions because Group II involves the fabrication of the apparatus utilizing processes such as electrodeposition and photolithographic etching and Group III involves isolation or separation of constituents via capture systems.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper. Moreover, since these inventions are distinct for the reasons given above and the search required for Group I is not required for Group II and the search required for Group II is further not required for Group III, restriction for examination purposes as indicated is proper. Literature search for each method and apparatus is distinct since the structural requirements of each invention are different. While searches would be expected to overlap, there is no reason to expect the searches to be coextensive.

During a telephone conversation with Mr. Brick Power on 7/7/99 a provisional election was made, without traverse, to prosecute the invention of Group I, claims 1-74 and 105-107. Affirmation of this election must be made by applicant in replying to this Office action. Claims 75-104 and 108-110 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Currently, claims 1-110 are subject to restriction and election requirement. Claims 75-104 and 108-110 have been withdrawn from further consideration as claims drawn to a non-elected invention. Claims 1-74 and 105-107 are pending and under examination.

Drawings

2. The drawings in this application are objected to by the Draftsperson (see PTO-948 attached) Correction is required. However, formal correction of noted defect can be deferred until application is allowed by the examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-74 and 105-107 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is unclear on what is meant by "sample application". It is unclear as to whether applicant intends to imply a void area within the first porous silicon region. Furthermore, claim 2 lacks proper antecedent basis and recites inconsistent language in reciting "said porous silicon region" since claim 1 refers to a specific "first" porous silicon region. Recitation of a "second" porous silicon region in the subsequent claims will further render the phrase inconsistent and indefinite.

Claim 3 is indefinite in reciting "defines a column" since it is unclear what is encompassed by the term "defines". See also claims 6, 30, 45, 51 first and second occurrence, 57 first and second occurrence, 64 and 65.

Claim 4 is indeterminate in scope in reciting "extends substantially linearly". As used in the claim, the term "substantially" lacks comparative basis for defining its metes and bounds.

Claim 7 is unclear in reciting "positioned along and contiguous with" since it does not specifically define how it is "positioned" relative to the first porous silicon region i.e. adjacent. See also claim 9.

Claim 10 is indefinite in reciting "disposed along" first and second occurrence since it does not specifically define what is encompassed by the term "disposed" as applied to the claim. Furthermore, it is unclear what the difference is between the phrases "position along" in the

previous claims and "disposed along" in this and subsequent claims. See also claims 12, 20, 25, 29, 30, 34, 50, 52, 56, 58 first and second occurrence, 66, and 106. Furthermore, it is unclear what the relationship is between the "first reaction region" and "second reaction region" in claim 10 and the "reactant region" in claims 7, 8, and 9. Please clarify.

Claim 18 is indefinite in reciting "a migration facilitator associated with said first porous silicon region" since it is unclear what is encompassed by the term "associated". See also claims 39, 40, 41, 42 first and second occurrence and 43.

Claim 19 is indefinite in reciting "a pump operatively associated with" since it is unclear what is encompassed by the phrase "operatively associated". See also claim 21.

Claim 42 is indefinite in reciting "said at least one capillary column and said at least one capillary column" because there is no apparent differentiation between the two elements and/or which "said capillary column" each one refers to.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-4, 12-25, 29, 30-34, 38-44, 50-65, 70, 73-74, and 105-107 are rejected under 35 U.S.C. 103(a) as being unpatentable over (1) Miura et al. (US 5,132,012) in view of (2) Wang et

al. (US 5,663,488), and in further view of (3) Northrup et al. (US 5,882,496) and Turner et al. (US 5,885,869).

Miura et al. disclose a miniaturized sample separator in the form of a liquid chromatograph comprising an analyzing chip in which the capillary flowpath is formed in a substrate and a field effect transistor detector is disposed downstream of the capillary (see Abstract). The substrate is made of silicon and further has an insulative membrane formed of silicon dioxide (see column 3, line 51 to column 4, line 7). Both the column for separation and the field effect transistor are formed intergrally with the substrate. After the silicon oxide layer has been formed on the capillary groove, a stationary phase is formed. Miura et al. further disclose a sample application area (introduction region) formed on the substrate (see column 4, lines 33-45). A switching-over valve which is connected to one end of the flow path in the sample application area (sample introduction pipe) selectively introduces the sample or a separation carrier solution into the flowpath. The sample is injected into the flowpath by an injector or a syringe manually or by an autosampler and the separation carrier solution is fed under pressure (vacuum source) by a feed pump and is discharged from a drain after having passed through the flowpath within the chip. Miura et al. further teach a seal plate such as borosilicate glass for sealing the opening portion of the groove portion to define the flow passage for the liquid sample. The liquid chromatograph further comprise a memory (control) device and an output device such as a data processor which is connected to the detector for detecting separated constituents (see column 5, line 63 to column 6, line 22). Figures 4A and 4B illustrate

an electrical conductivity detector which comprise voltage application and current detection components, i.e. electrodes. Figure 9 shows a schematic view of the overall flow passage of the liquid chromatograph. Figure 9 shows the principle or concept of the entire flowpath or passage of the liquid chromatograph.

Miura et al. fail to teach integration of a migration facilitator and thermal detector. Miura et al. further fail to teach incorporation of porous silicon and/or hemispherical grain silicon into the separation columns. Miura et al. also fail to teach an electrophoretic device.

Wang et al. disclose a migration facilitator (pumping assembly) incorporated into a separation column and thermal device for use in selective control of thermal isolation of the thermal zone as well as effecting selective amount of gas pressure in an enclosed cavity (see Abstract). The pumping element comprises an element in the form of a tubular or planar palladium structure. Wang et al. disclose that the migration facilitator controls the extent of thermal isolation by changing the gas pressure in the cavity thereby changing the amount of heat transfer between the separation column and housing so as to reduce the need for operation of the thermal device (see column 2, lines 1-54). The migration facilitator also includes a control (check) valve for venting or purging gasses form the closed cavity, a vacuum (or near vacuum) source for use in high vacuum pumps for altering the concentration of gas within the cavity volume (see column 4, lines 4-59). Wang further disclose that a thermal conductivity detector is integrated into the chromatograph for determining physicochemical properties of the fluid stream which exits the separation column (see column 10, line 60 to column 11 line 33).

Northrup et al. disclose fabrication and use of porous silicon structures to increase surface area of miniaturized electrophoresis devices and filtering or control flow devices (see Abstract). Northrup et al. specifically disclose that porous silicon which is fabricated from crystalline silicon have very small pore diameters so that they can be produced with relatively high degree of uniformity and control (see column 1, lines 27-55). Northrup et al. teach that because of its high surface area and specific pore size, porous silicon can be utilized for a variety of applications on a miniature scale for significantly augmenting adsorption, vaporization, desorption, condensation, and flow of liquids and gasses while maintaining the capability of modification such as being doped or coated using conventional integrated circuit and micromachining (see Summary). Electrodes within or adjacent the porous membrane can be used to control flow or electrically charged biochemical species such as in electrophoresis (see column 5, lines 21-67). Figure 3 illustrates porous silicon embodiment on a controlled flow interface device. Figure 8 illustrates a porous silicon electrophoresis device. A negative electrode is formed at one end (inlet) of the porous silicon column and a positive electrode is formed is formed at an opposite end (outlet) of porous silicon columns, thereby forming microelectrophoresis channels (see column 7, lines 38-50).

Turner et al. disclose a method for uniformly doping hemispherical grain polycrystalline silicon and fabricating semiconductor wafers which facilitates the doping of a top roughened polycrystalline silicon layer independently from the doping of a bottom polycrystalline silicon layer of a semiconductor substrate (see Abstract). Initially, a semiconductor substrate having a

silicon dioxide layer formed superadjacent a polycrystalline layer is provided, preferably in a chamber. Subsequently, a doped rough silicon layer is formed in situ superadjacent the silicon dioxide layer which is accomplished by depositing a silicon layer superadjacent the silicon dioxide layer and exposing the silicon layer to a source gas. The step of roughening is achieved by vacuum annealing an amorphous layer using rapid thermal chemical vapor deposition techniques or low pressure chemical vapor deposition (see column 3, lines 7-23).

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute porous silicon as taught by Northrup et al. and the hemispherical grain silicon as taught by Turner et al. into the separation column of Miura et al. because Miura et al. specifically indicated difficulty in miniaturization of liquid column chromatograph and Northrup et al. specifically taught that use of porous silicon with specifically small uniform pore size can significantly increase surface area of a variety of applications such as electrophoresis devices in the miniature scale. Furthermore, it would have been obvious to one of ordinary skill in the art at time of the invention to incorporate therein, a migration facilitator as taught by Wang et al. because Wang et al. specifically suggested application of his pump assembly to other analytical instruments such as liquid or gas chromatographic systems capable of regulated flow. One of ordinary skill in the art at the time of the invention would have been motivated to incorporate the teachings of Northrup et al. and Turner et al. into the liquid chromatography device of Miura et al. with the migration facilitator taught by Wang et al. incorporated therein to effect selective pressurization and thermal isolation, because of the advantage introduced by the use of porous

silicon as taught by Northrup et al. in significantly augmenting adsorption, vaporization, desorption, condensation, and flow of both liquid and gas in applications of miniature scales.

5. Claims 1-12, 14-17, 25-38, 42-52, 54-69, 71-74 and 105-107 are rejected under 35 U.S.C. 103(a) as being unpatentable over (1) Miura et al. (US 5,132,012) in view of (2) Swedberg et al. (US 5,571,410) and Sunzeri (US 5,536,382) and in further view of (3) Northrup et al. (US 5,882,496) and Turner et al. (US 5,885,869).

Miura et al., Northrup et al., and Turner et al. have been discussed supra. Miura et al. fails to teach incorporation of reaction region into the stationary phase in order to form a capture system. Furthermore, Miura et al. fails to teach use of internal reference or control.

Swedberg et al. teach a miniaturized planar column device for integrated sample analysis of analytes (see column 8, lines 5-38). Swedberg et al. specifically teach a stationary phase (sample treatment component) which performs a filtration function filled with a biocompatible porous medium of particles into which a capture function has been incorporated therein (see column 27, lines 33-61 and Example 1). Swedberg et al. also disclose a "LIGA" process which is used to refer to a process of fabricating microstructures having high aspect ratios and increased structural precision in order to create desired uniformity in microstructures such as channels ports, apertures, and microalignment means (see column 13, lines 9-33).

Sunzeri discloses analysis of constituents of human biological fluids using capillary electrophoresis. Sunzeri specifically teaches the use of standard control to provide a standard for

quantitation (see column 9, lines 28-67). Sunzeri further teaches that quantitation using internal and external standards is beneficial in assays where the sample matrix affects fluorescence sample quenching (see column 10, lines 1-34).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the stationary phase in the chromatographic separation apparatus and detection system taught by Miura et al., with porous and hemispherical grain silicon as taught by Northrup et al. and Turner et al. incorporated therein, one that effects biocompatibility into the matrix as taught by Swedberg et al. in order to achieve performance of both filtration and capture function because Swedberg et al. specifically suggested potential application of his teachings in monitoring biological analyses as applied to liquid phase separation devices in the miniature scales. One of ordinary skill in the art would have been motivated to incorporate the teachings of both Northrup et al. and Turner et al. into the separation device of Miura et al. with biocompatible modification as taught by Swedberg et al. because of the advantage introduced by the use of porous silicon in significantly augmenting adsorption, vaporization, desorption, condensation, and flow of both liquid or gas in applications of miniature scales thereby producing a highly versatile miniaturized chromatographic device capable of both enhanced partitioning and complexation reactions. Furthermore, with the advent of silicon micromachining and LIGA in teachings of Swedberg, one of ordinary skill in the art would have expected reasonable success in fabricating multiple separation columns or channels with a high degree of uniformity and precision in order to allow accurate comparative and correlative

measurement of sample results in comparison to an internal control, a reference, or a standard with known measurement levels as those taught by Sunzeri, because quality control monitoring is a standard practice and a well known art for monitoring the functionality, accuracy, and precision of assays in various laboratory apparati.

For reasons aforementioned, no claims are allowed.

Remarks

6. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

Anderson et al. (US 5,922,591) disclose a miniaturized integrated nucleic acid diagnostic device capable of sample acquisition, storage, sample preparation, and analysis within a single integrated unit.

Kaltenbach et al. disclose miniaturized column devices for bioanalytical systems (see Figure 8). Kaltenbach et al. specifically teach a stationary phase (sample treatment component) which performs a filtration function. The medium is biocompatible and is designed to serve a capture function (see column 17, lines 3-31). The matrix includes a biological affiant such as antibody, antigen, lectin, enzyme substrate, or capture oligonucleotide.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The

examiner can normally be reached on Monday to Thursday from 7:00 AM to 4:30 PM. The examiner can also be reached on alternate Fridays from 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Jr Gabel 7/19/99

Gailene R. Gabel
Patent Examiner
Art Unit 1641

Rodney P Swartz PhD

RODNEY SWARTZ
PATENT EXAMINER